

Normal cellular response to chemoattractant signaling.

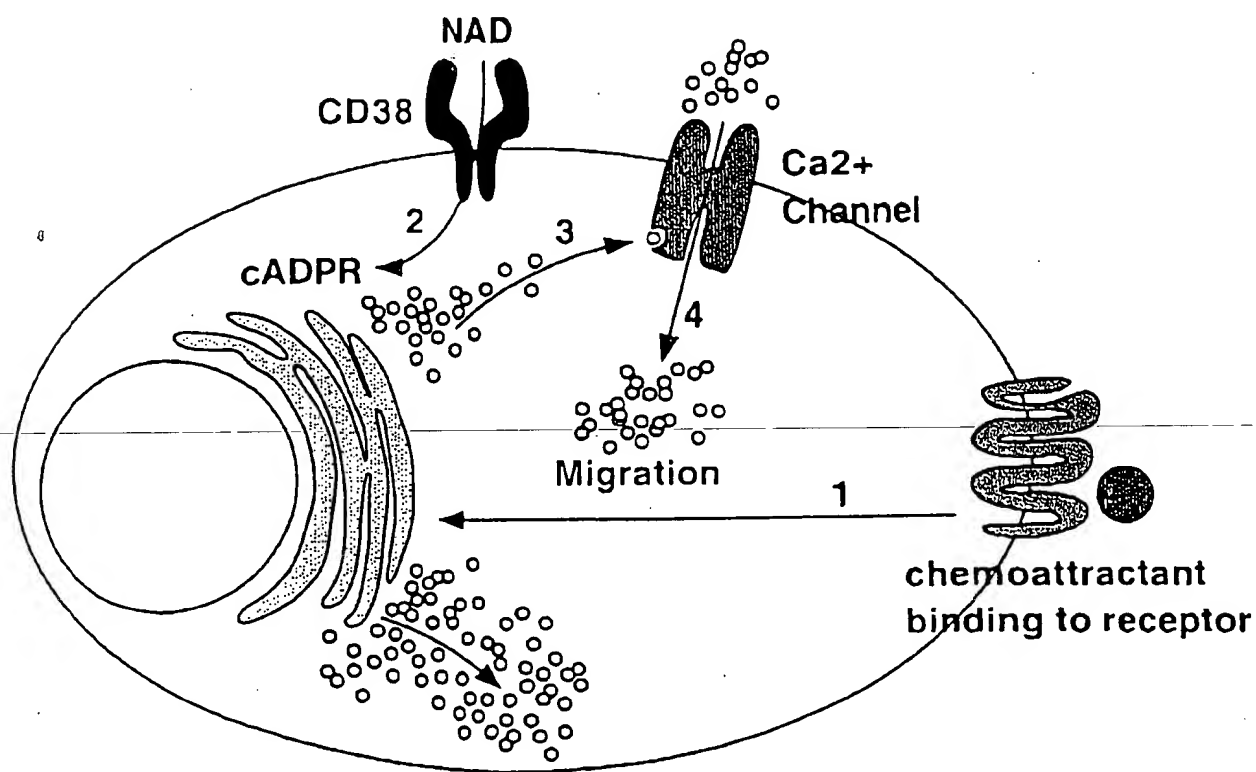


Figure 1

Inhibitors of cADPR production
by CD38 prevent capacitative
 Ca^{2+} entry and chemoattractant
induced migration

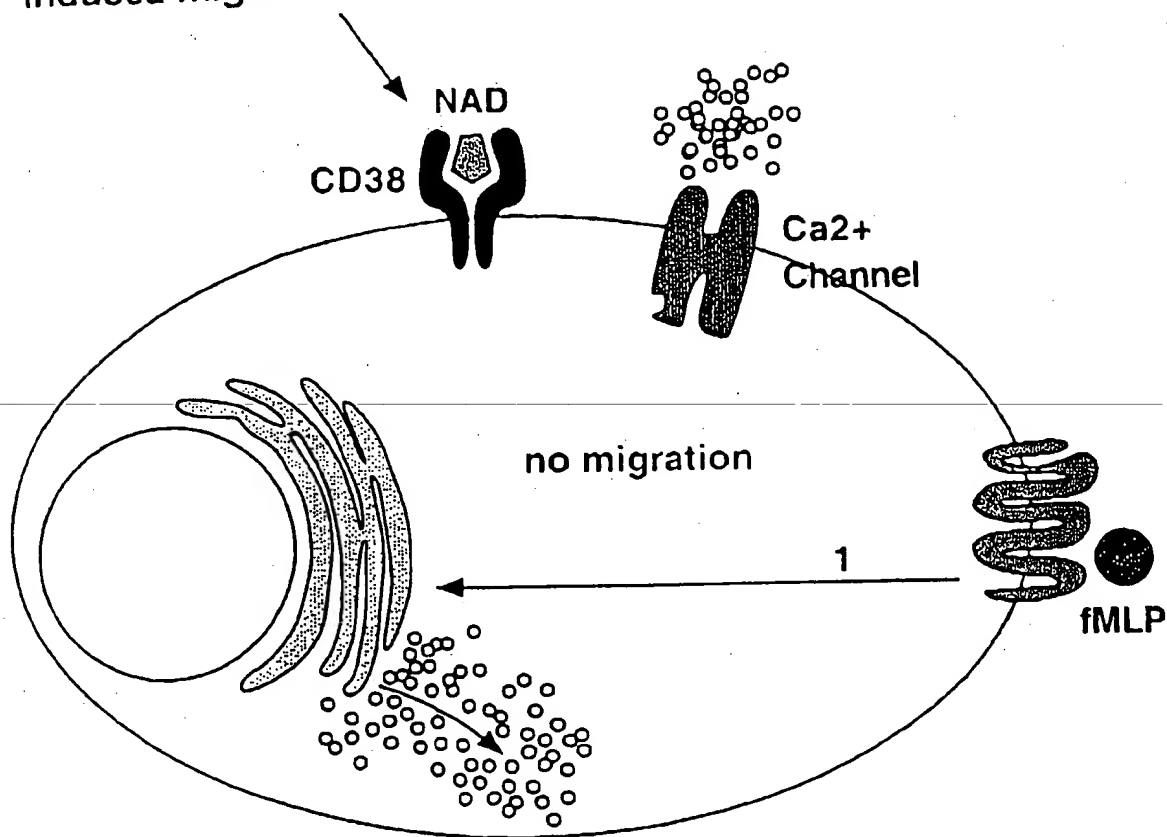


Figure 2

Proteins that regulate CD38 enzyme activity (screens will identify compounds that activate or inactivate these proteins)

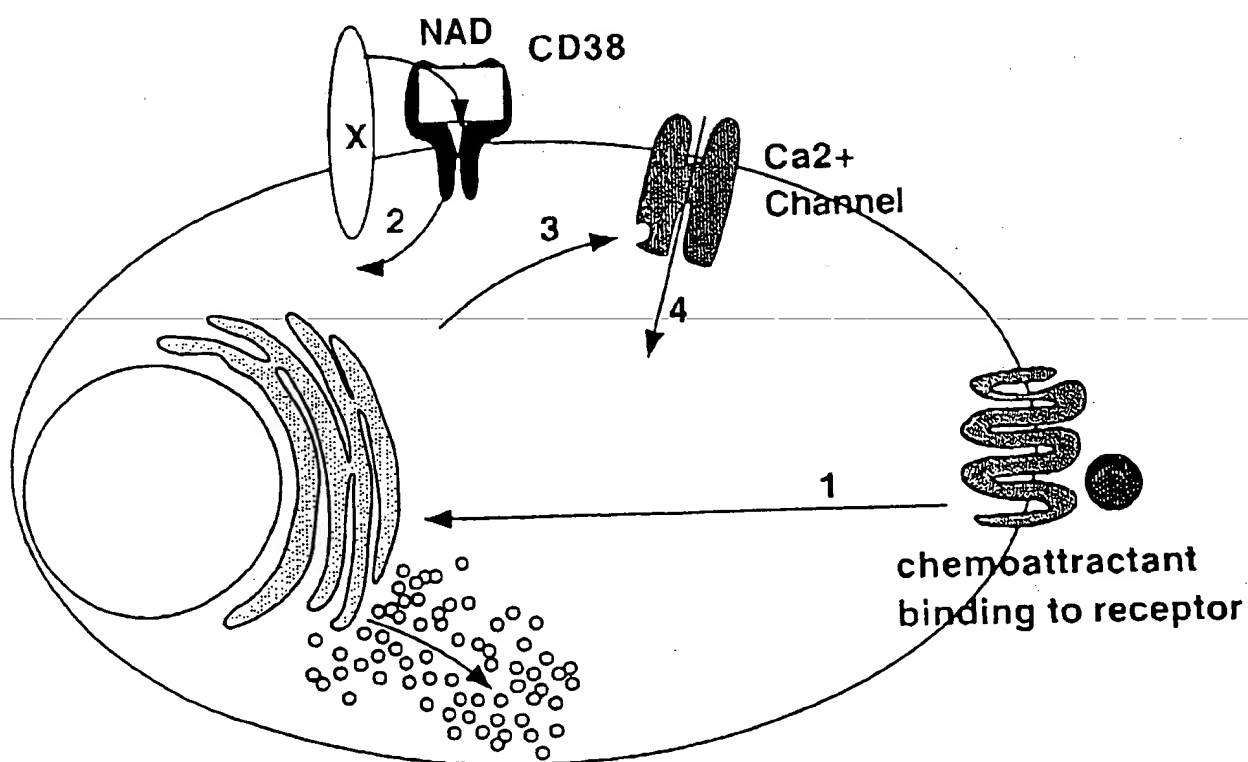


Figure 3

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Proteins that regulate CD38 expression (screens will identify compounds that activate or inactivate these proteins)

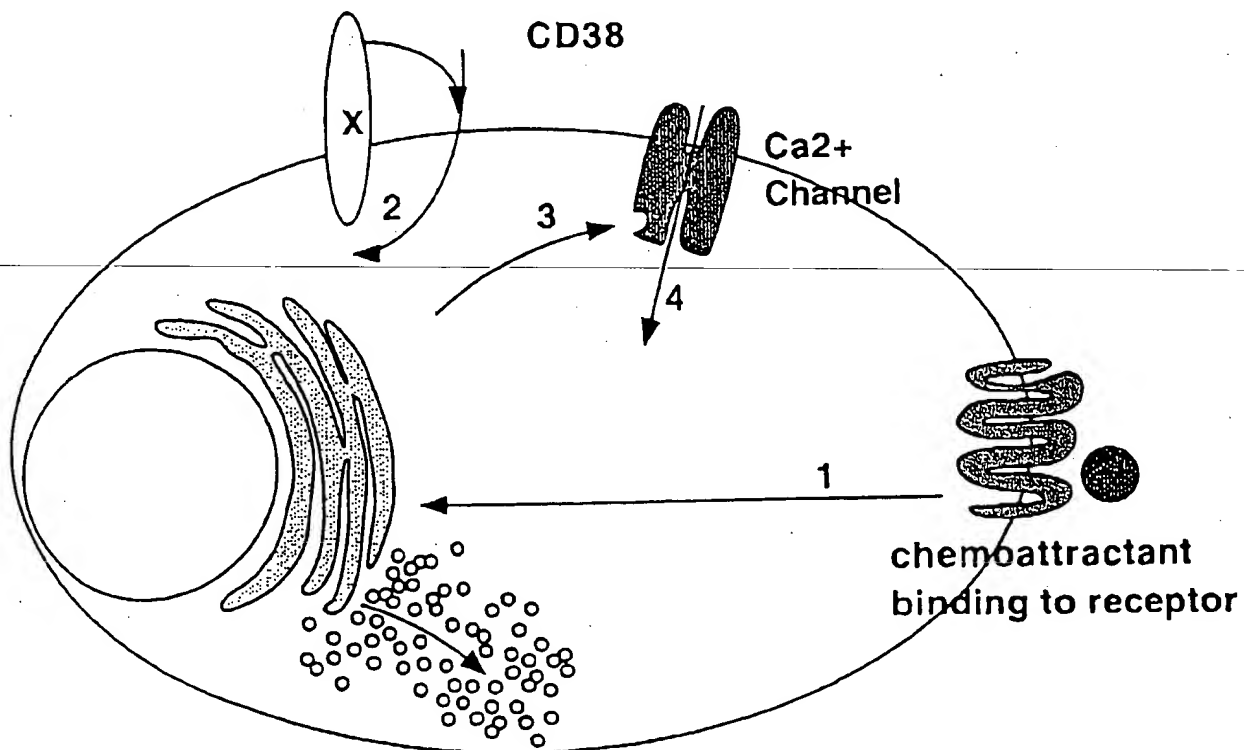


Figure 4

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Alternative substrates for CD38 may
generate inhibitors of cADPR and
prevent capacitative Ca^{2+} release

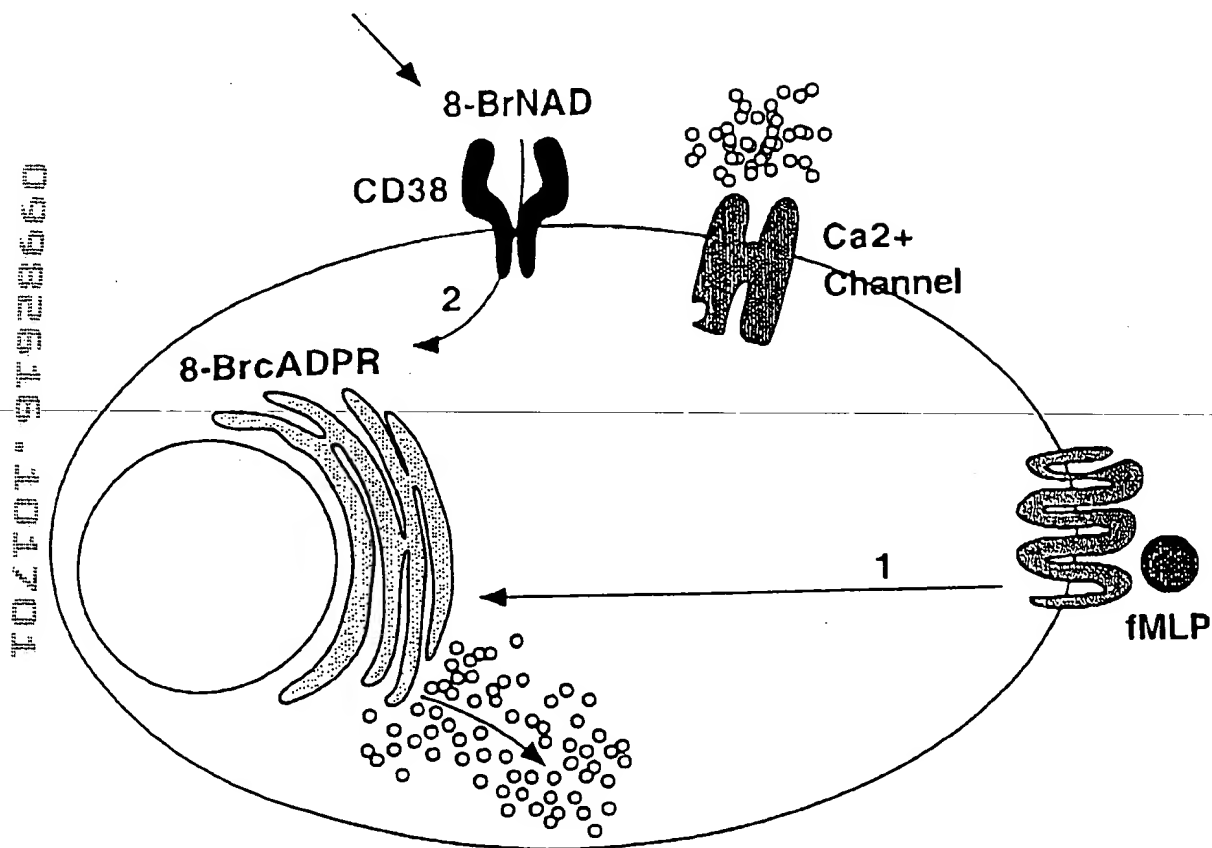


Figure 5

Inhibitors of cADPR binding
block capacitative Ca^{2+} influx

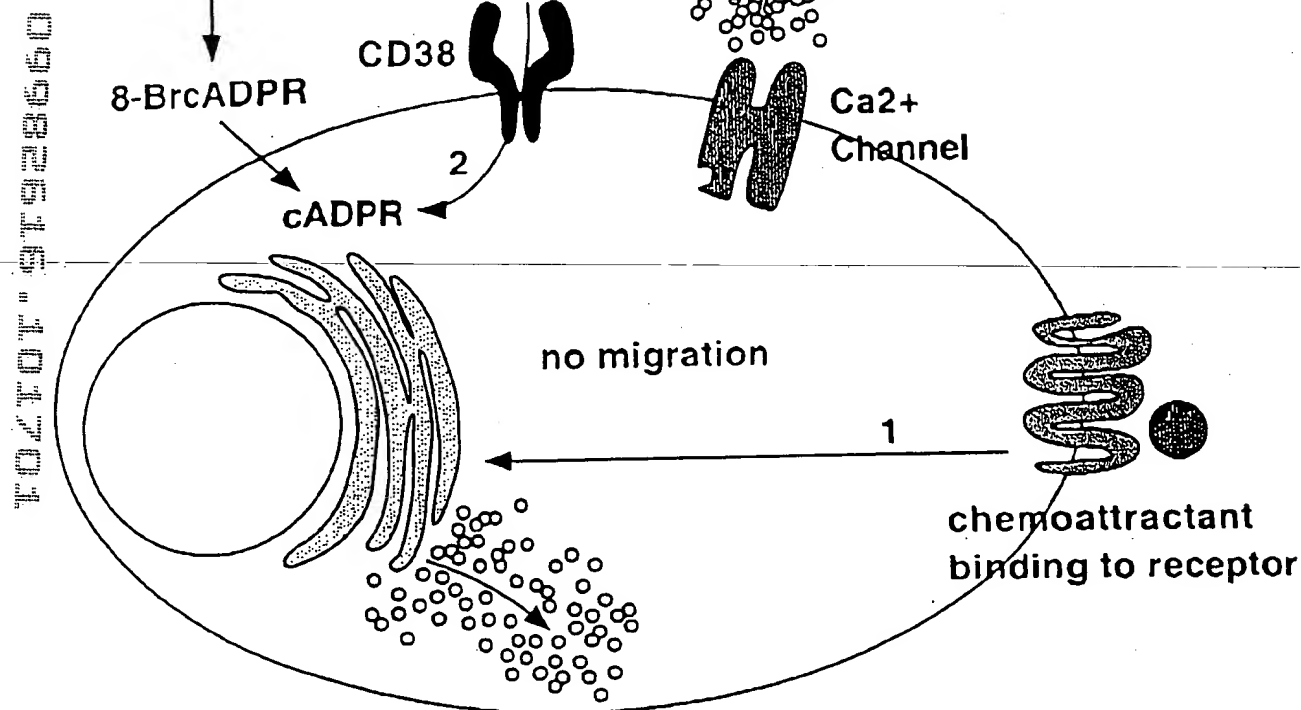
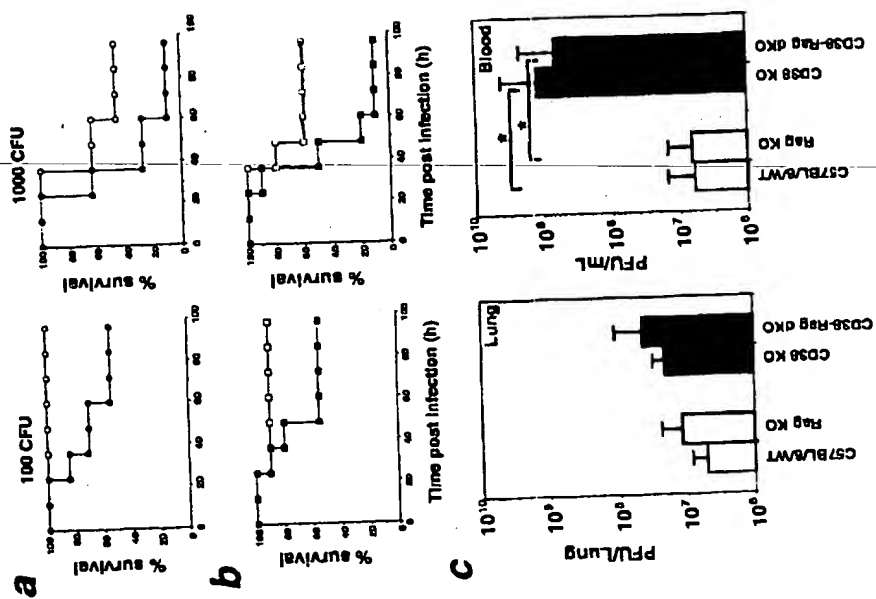


Figure 6

Figure 7 A-C



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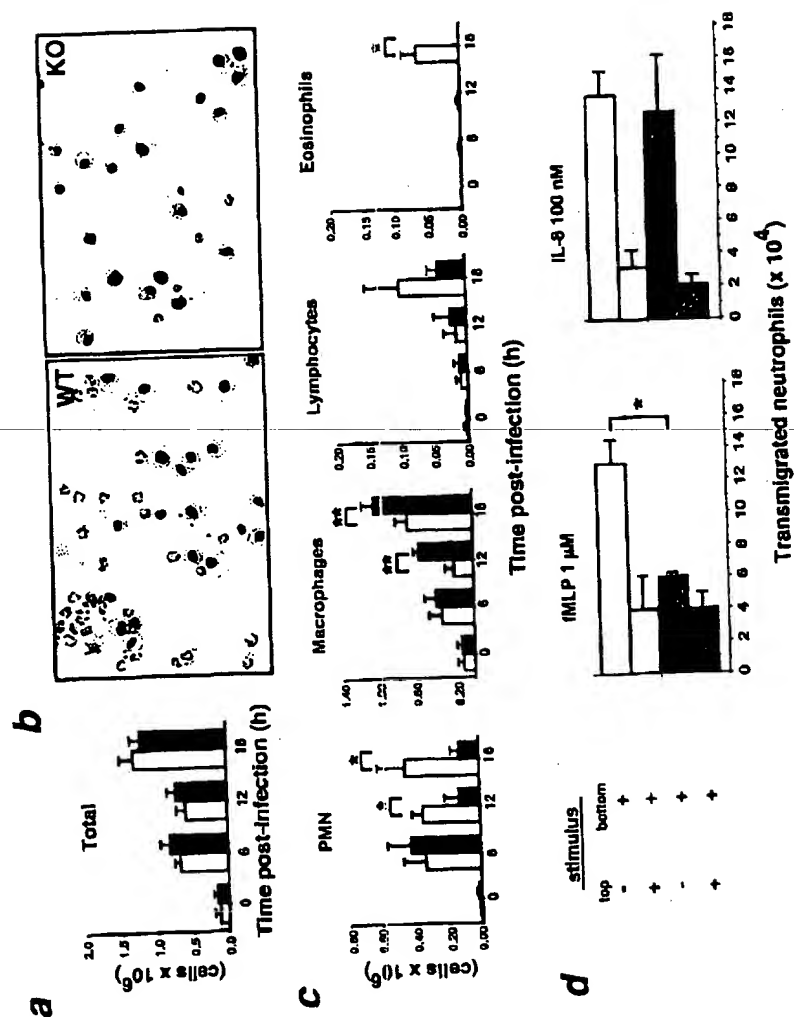


Figure 8 A-D

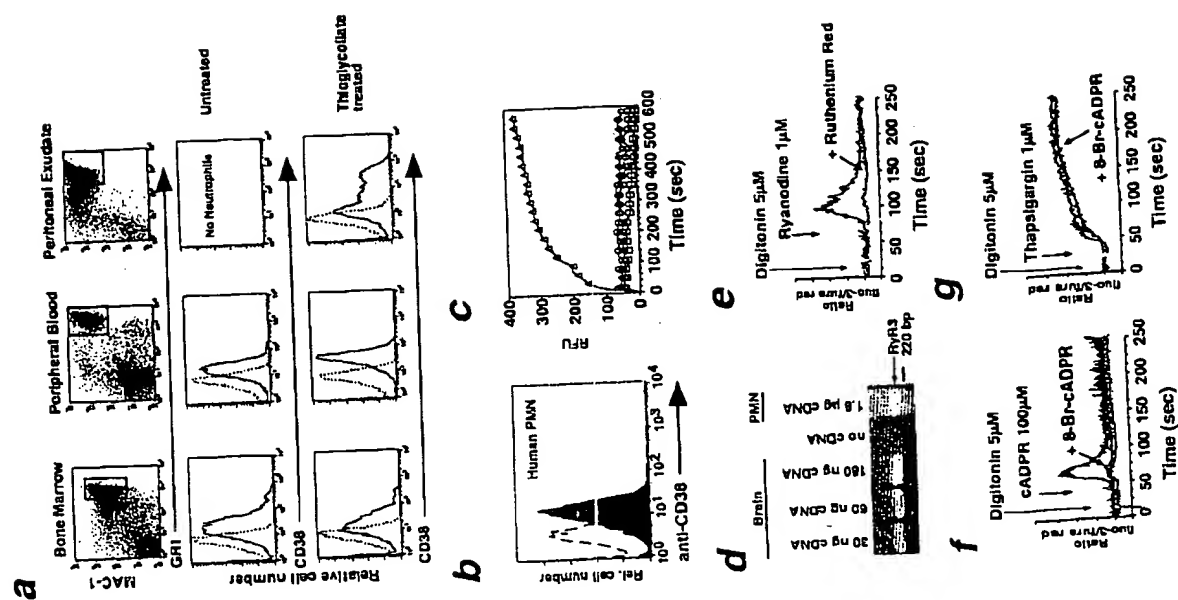


Figure 9A-6

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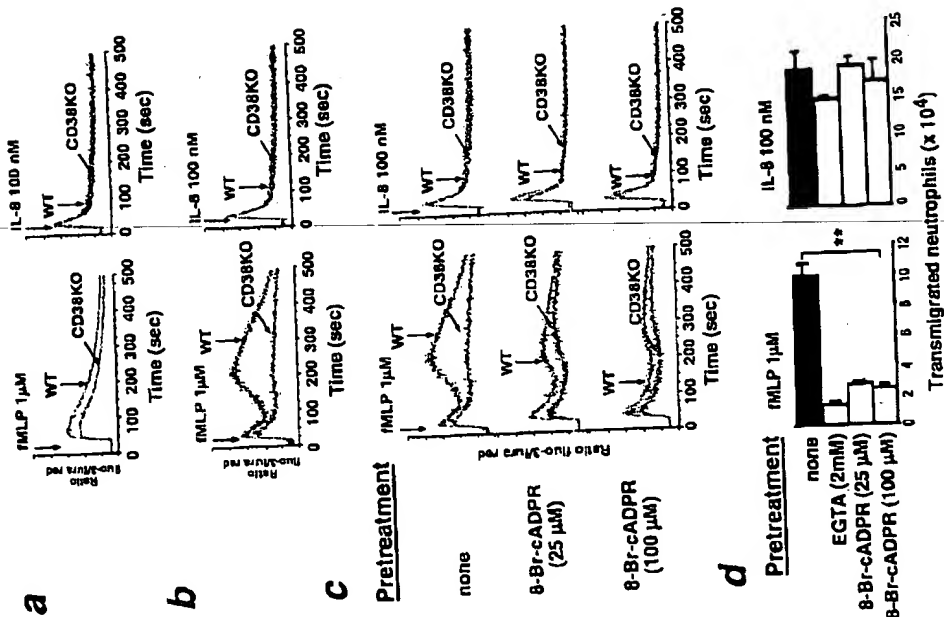


Figure 10 A-D

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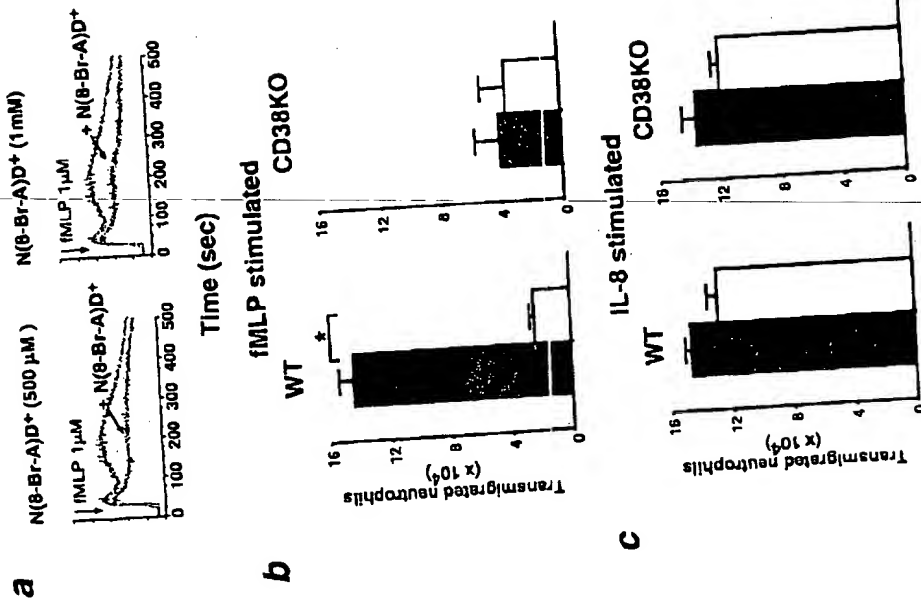


Figure 11A2

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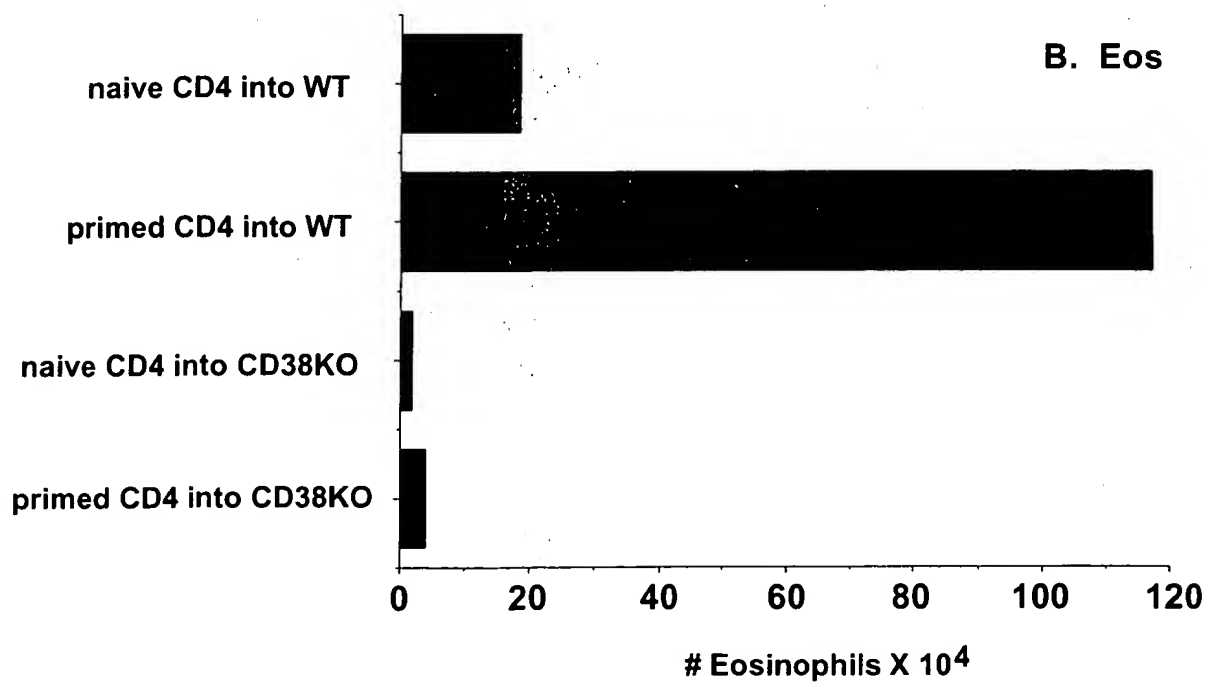
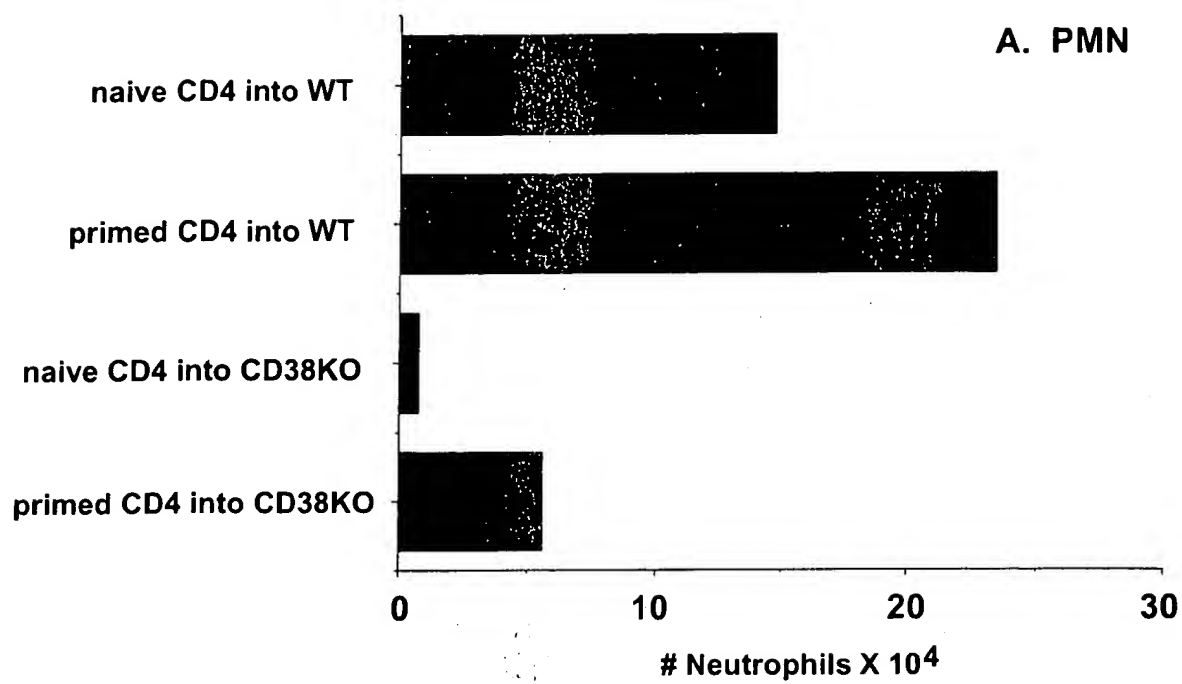


Figure 12

Figure 13A

Consensus	GGAAAGAACG TAGACATATA TTGTTATATA GATTGTTCA GTTATTTTC	50
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	-----	
SM38	GGAAAGAACG TAGACATATA TTGTTATATA GATTGTTCA GTTATTTTC	50
Consensus	ACAATCTTTT AATTCAAATA ATGATGAACG TAATATTGTT TCTTACTTTA	100
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	-----	
SM38	ACAATCTTTT AATTCAAATA ATGATGAACG TAATATTGTT TCTTACTTTA	100
Consensus	TCAAATATTT TTGTCTTTAA CTCTGCACAA CATCAAATAA ACTTACTTAG	150
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	-----	
SM38	TCAAATATTT TTGTCTTTAA CTCTGCACAA CATCAAATAA ACTTACTTAG	150
Consensus	TGAAATAGTA CAATCACGAT GTACTCAGTG GAAGGTTGAA CATGGAGCTA	200
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	-----	
SM38	TGAAATAGTA CAATCACGAT GTACTCAGTG GAAGGTTGAA CATGGAGCTA	200
Consensus	CTAATATAAG TTGTAGTGAG ATCTGGAATT CATTGAAAG CATTTTACTT	250
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	-----	
SM38	CTAATATAAG TTGTAGTGAG ATCTGGAATT CATTGAAAG CATTTTACTT	250
Consensus	TCAACTCATA CTAAATCAGC ATGTGTTATG AAATCAGGGT TATTCGATGA	300
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	-----	
SM38	TCAACTCATA CTAAATCAGC ATGTGTTATG AAATCAGGGT TATTCGATGA	300
Consensus	TTTTGTTTAT CAATTGTTTG AATTGGAACA ACAACAACAA CAGCGACACC	350
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	-----	
SM38	TTTTGTTTAT CAATTGTTTG AATTGGAACA ACAACAACAA CAGCGACACC	350
Consensus	ACACAATTCA AACGGAACAA TACTTCCATT CTCAAGTGAT GAACATCATT	400
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	-----	
SM38	ACACAATTCA AACGGAACAA TACTTCCATT CTCAAGTGAT GAACATCATT	400
Consensus	CGTGGAATGT GTAAACGTCT TGGAGTATGT CGTTCTCTAG AAACATCATT	450
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	-----	
SM38	CGTGGAATGT GTAAACGTCT TGGAGTATGT CGTTCTCTAG AAACATCATT	450
	-GGAGTATGT CGTTCTCTAG AAACATCATT	29
	CGTGGAATGT GTAAACGTCT TGGAGTATGT CGTTCTCTAG AAACATCATT	450

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Figure 13B

Consensus	TCCAGGATAT CTGTTTGATG AATTGAATTG GTGTAATGGC AGTTTAACAG	500
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	TCCAGGATAT CTGTTTGATG AATTGAATTG GTGCAATGGC AGTTTAACAG	79
SM38	TCCAGGATAT CTGTTTGATG AATTGAATTG GTGTAATGGC AGTTTAACAG	500
Consensus	GCAACACAAA ATACGGGACT GTATGTGGAT GCGATTATAA AAGTAATGTT	550
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	GCAACACAAA ATACGGGACT GTATGTGGAT GCGATTATAA AAGTAATGTT	129
SM38	GCAACACAAA ATACGGGACT GTATGTGGAT GCGATTATAA AAGTAATGTT	550
Consensus	GTTTCATGCGT TCTGGCAAAG TGCTTCGGCT GAGTATGCCA GGAGAGCATC	600
EST AW017229 comp	-----	
EST A1067047 comp	-----	
EST N20756	GTTTCATGCGT TCTGGCAAAG TGCTTCGGCT GAGTATGCCA GGAGAGCATC	179
SM38	GTTTCATGCGT TCTGGCAAAG TGCTTCGGCT GAGTATGCCA GGAGAGCATC	600
Consensus	TGGTAACATC TTTGTGGTAC TGAATGGCTC GGTCAAAGCT CCATTTAATG	650
EST AW017229 comp	TGGTAACATC TTTGTGGTAC TGAATGGCTC GGTCAAAGCT CCATTTAATG	74
EST A1067047 comp	-----	
EST N20756	TGGTAACATC TTTGTGGTAC TGAATGGCTC GGTCAAAGCT CCATTTAATG	229
SM38	TGGTAACATC TTTGTGGTAC TGAATGGCTC GGTCAAAGCT CCATTTAATG	650
Consensus	AAAATAAAAC TTTTGGA AAA ATAGAACTAC CATTGGTTAA AACATCCTCG	700
EST AW017229 comp	AAAATAAAAC TTTTGGA AAA ATAGAACTAC CATT-GTTAA AACATCCTCG	123
EST A1067047 comp	-----	
EST N20756	AAAATAAAAC TTTTGGA AAA ATAGAACTAC CATTGGTTAA AACATCCTCG	279
SM38	AAAATAAAAC TTTTGGA AAA ATAGAACTAC CATTG-TTAA AACATCCTCG	699
Consensus	AGTACAACAA TTAACAGTGA AATTAGTTCA TAGTTTGGAA GATGTAAATA	750
EST AW017229 comp	AGTACAACAA TTAACAGTGA AATTAGTTCA TAGTTTGGAA GATGTAAATA	173
EST A1067047 comp	-----	
EST N20756	A-----	280
SM38	AGTACAACAA TTAACAGTGA AATTAGTTCA TAGTTTGGAA GATGTAAATA	749
Consensus	ACCGACAAAC ATGTGAATCG TGGAGTCTGC AAGAACTTGC AAACAAGCTG	800
EST AW017229 comp	ACCGACAAAC ATGTGAATCG TGGAGTCTGC AAGAACTTGC AAACAAGCTG	223
EST A1067047 comp	-----	
EST N20756	-----	280
SM38	ACCGACAAAC ATGTGAATCG TGGAGTCTGC AAGAACTTGC AAACAAGCTG	799
Consensus	AACTCTGTAC ATATTCCTTT TCGTTGCATT GACGATCCTT TAGAGTTCAG	850
EST AW017229 comp	AACTCTGTAC ATATTCCTTT TCGTTGCATT GACGATCCTT TAGAGTTCAG	273
EST A1067047 comp	-----	
EST N20756	-----	280
SM38	AACTCTGTAC ATATTCCTTT TCGTTGCATT GACGATCCTT TAGAGTTCAG	849
Consensus	ACATTATCAA TGCATTGAAA ATCCTGGCAA ACAACTATGT CAGTTTTCAG	900
EST AW017229 comp	ACATTATCAA TGCATTGAAA ATCCTGGCAA ACAACTATGT CAGTTTTCAG	323
EST A1067047 comp	-----	
EST N20756	-----	280
SM38	ACATTATCAA TGCATTGAAA ATCCTGGCAA ACAACTATGT CAGTTTTCAG	899

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Figure 13C

Consensus

EST AW017229 comp
EST A1067047 comp
EST N20756
SM38

CTTCGACGAG	GTCAAACGTC	GAGACATTAC	TCATACTTTT	TCCGCTAGTC
CTTCGACGAG	GTCAAACGTC	GAGACATTAC	TCATACTTTT	TCCGCTAGTC
CTTCGACGAG	GTCAAACGTC	GAGACATTAC	TCATACTTTT	TCCGCTAGTC
CTTCGACGAG	GTCAAACGTC	GAGACATTAC	TCATACTTTT	TCCGCTAGTC

950
373
87
280
949

Consensus

EST AW017229 comp
EST A1067047 comp
EST N20756
SM38

ATTTGTTTAA	CTTTTATAC	TTCCATGAAT	TGAAATAACT	TTTCAGAACT
ATTTGTTTAA	CTTTTATAC	TTCCATGAAT	TGAAATAACT	TTTCAGAACT
ATTTGTTTAA	CTTTTATAC	TTCCATGAAT	TGAAATAACT	TTTCAGAACT
ATTTGTTTAA	CTTTTATAC	TTCCATGAAT	TGAAATAACT	TTTCAGAACT

1000
423
137
280
999

Consensus

EST AW017229 comp
EST A1067047 comp
EST N20756
SM38

AACTTTGAA	CAGAGAAAGA	GAACAATGAT	AATAAAGGAA	TAGGMCATTA
AACTTTGAA	CAGAGAAAGA	GAACAATGAT	AATAAAGGAA	TAGGCCATTA
AACTTTG--	-----	-----	-----	-----
AACTTTGAA	CAGAGAAAGA	GAACAATGAT	AATAAAGGAA	TAGGACATTA

1050
473
145
280
1049

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Figure 14

GGAAAGAACGTAGACATATATTGTTATATAGATTGTTTCAGTTATTTTTTACAATCTTTTAATTCAAATA 70
E R T T Y I V I I C S V I F H N L L I Q I

ATGATGAACGTAATATTGTTTCTTACTTTATCAAATATTTTGTCTTTAACTCTGCACAACATCAAATAA 140
M M N V I L F L T L S N I F V F N S A Q H Q I

ACTTACTTAGTGAAATAGTACAATCACGATGTACTCAGTGAAGGTTGAACATGGAGCTACTAATATAAG 210
N L L S E I V Q S R C T Q W K V E H G A T N I S

TTGTAGTGAGATCTGGAATTCATTTGAAAGCATTTTACTTTCAACTCATACTAAATCAGCATGTGTTATG 280
C S E I W N S F E S I L L S T H T K S A C V M

AAATCAGGGTTATTTCGATGATTTTGTATCAATTGTTTGAATTGGAACAACAACAACAGCGACACC 350
K S G L F D D F V Y Q L F E L E Q Q Q Q Q R H

ACACAATTCAAACGGAACAATACTTCCATTCTCAAGTGATGAACATCATTGCGTGAATGTGTAACGTCT 420
H T I Q T E Q Y F H S Q V M N I I R G M C K R L

TGGAGTATGTCGTTCTCTAGAACTACATTTCCAGGATATCTGTTTGATGAATTGAATTGGTGTAAATGGC 490
G V C R S L E T T F P G Y L F D E L N W C N G

AGTTTAACAGGCAACACAAAATACGGGACTGTATGTGGATGCGATTATAAAAGTAATGTTGTTTCATGCGT 560
S L T G N T K Y G T V C G C D Y K S N V V H A

TCTGGCAAAGTGCTTCGGCTGAGTATGCCAGGAGAGCATCTGGTAACATCTTTGTGGTACTGAATGGCTC 630
F W Q S A S A E Y A R R A S G N I F V V L N G S

GGTCAAAGCTCCATTTAATGAAAATAAAAGTTTGGAAAAATAGAAGTACCATTGTTAAAACATCCTCGA 700
V K A P F N E N K T F G K I E L P L L K H P R

GTACAACAATTAACAGTGAAATTAGTTCATAGTTTGAAGATGTAAATAACCGACAAACATGTGAATCGT 770
V Q Q L T V K L V H S L E D V N N R Q T C E S

GGAGTCTGCAAGAACTTGCAAACAAGCTGAACTCTGTACATATTCTTTTTCGTTGCATTGACGATCCTTT 840
W S L Q E L A N K L N S V H I P F R C I D D P L

AGAGTTCAGACATTATCAATGCATTGAAAATCCTGGCAAACAACATATGTCAGTTTTTCAGCTTCGACGAGG 910
E F R H Y Q C I E N P G K Q L C Q F S A S T R

TCAAACGTCGAGACATTACTCATACTTTTTCCGCTAGTCATTTGTTTAACTTTTTTATACTTCCATGAATT 980
S N V E T L L I L F P L V I C L T F Y T S M N

GAAATAACTTTTCAGAACTAAACTTTGAACAGAGAAAGAGAACAATGATAATAAAGGAATAGGACATTAA 1050
N N F S E L N F E Q R K R T M I I K E D I N

TGAAAAAAAAAAAAAAAAAAAAA 1073
E K K K K K K

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Consensus	M.....L.....S....I.....L.....RC.....	50
<i>Aplysia</i> cd38p	MSPVAIVACV CLAVTLTRIS PSEAIPTPE LQNVFLGRCK DYEITRYLTI	50
SM38p	M--MNVLFL TLSNIFVFN A QHQI---NL LSEIVQSRC QWKVEH----	41
ConsensusC...W..F.....K..C...G...DF.....	100
<i>Aplysia</i> cd38p	LPRVKSDCRA LWTNFFKAFA F---KAPCNL DLGSYKDDFFQ RAQQTLPKNN	97
SM38p	-GATNISCSE IWNSEFESILL STHTKSAQVM KSGLFDDFVY QLFELEQQQQ	90
Consensus*.....LE.T.PGY...L.WC..	150
<i>Aplysia</i> cd38p	VMFWSGVYDE --AHDF--- ADDGRKYI-- -TLEDTLPGY MLNSLWCGQ	138
SM38p	QRHHTIQTEQ YFHSQVMNII RGMCKRLGVC RSLETTTFPGY LFDELWENG	140
ConsensusVC....D....FW..A S..YA..A.G.....GS.	200
<i>Aplysia</i> cd38p	RDKPGFNQK- VQPDFKDCPV QARESFWGTA SSSYAHSAEG DVTYMDGSSN	187
SM38p	SLTGNTKYGT VC--GCDYKS NVVHAFWQSA SAEYARRASG NIFVVLNGS-	186
Consensus*.....FGK.ELP.L....V.....H.L....C...SL	250
<i>Aplysia</i> cd38p	PKVPAYRPDS FFGKYELPNL TNK-VTKVKV IVLHQLGQKI I-ERCAGASL	235
SM38p	-VKAPFNENK TFGKIELPLL KHPRVQQLTV KLVHSLEDVN NRTGESWSL	236
Consensus	..L.....F.C...P.....C...NP....CQ.....	300
<i>Aplysia</i> cd38p	LDLEMVVKAK KFGFDCEVNP KSVLFLLCAD NPNARECQLA KRYRYIA---	282
SM38p	QELANKLSNV HIPERCIDDP LEFRHYQIE NPGKQLCQFS ASTRSNVETL	286
Consensus	317
<i>Aplysia</i> cd38p	-----	282
SM38p	LILFPLVICL TFYTSMN	303

Consensus	M..... ..IL...L..Q.	50
Human CD38	MANCEFPVPS GDKPCCRLSR RAQLCLGVSI LVLILVVVLA VVVPRWRQQW	50
SM38p	M----- MNVILFLTLS NIFVFNSAQ-	20
Consensus E.V..RC... ..C...W..F.S.H.K.	100
Human CD38	SGPGTTKRFP ETVLARCVKY TEIHPEMRHV DCQSVDFAFK GAFIS---KH	97
SM38p	---HQINLLS EIVQSRCTQW -KVEHGATNI SCSEIWNSFE SILLSTHTKS	66
Consensus	.C..... ..YQ..... ..S.....	150
Human CD38	PCNITEED-- ---YQPLMKL GTQTVPCKNI L----LWSRI KDLAHQFTQV	138
SM38p	ACVMKSLGFD DFVYLFELE QQQQRHHTI QTEQYFHSQV MNIIRGMCKR	116
Consensus *LE.T ..GYL.D.L. WC...T... .Y...C.... ..C....N.V	200
Human CD38	QRDMFTLEDIT LLGYLADDIT WCGEFNTSKI NYQS-CPDWR KDC--SNNPV	185
SM38p	LGVCRSLETIT FPGYLFDELN WCNGLSLTGNT KYGTVCG--- --CDYKSNVV	161
Consensus	..FW...S... .A..A..... V.LNGS.... F..N.TFG.. * E...L....V	250
Human CD38	SVFWKTVSRR FAEAACDVVH VMLNGSRSKI FDKNSTFGSV EVHNLOPEKV	235
SM38p	HAFWQSAAE YARRASGNIF VVLNGSVKAP FNENKTFGKI ELPLLKHPRV	211
Consensus	Q.L....H.R..CEL..I.F. C.....	300
Human CD38	QTLEAWVIHG GRE-DSRDLC QDPTIKELES IISKRNIQFS CKNIYRPDKF	284
SM38p	QQLTVKLVHS LEDVNNRQTC ESWSLQELAN KLNSVHIPER CIDDPLEFRH	261
Consensus	.QC..NP... .C..... ..TS ..	342
Human CD38	LQCVKNPEDS SC----- -----TS EI	300
SM38p	YQCIENPGKQ LCQFSASTRS NVETLLILFP LVICLTFTYS MN	303

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MMNVILFTL	SNIFVFNSAQ	HQINLSEIV	QSRCTQWKVE	HGATNI	SCSE	50
IWNSFESILL	STHTKSACVM	KSGLEDDFVY	QLFELEQQQQ	QRHHTI	QTEQ	100
YFHSQVMNII	RGMCRLGVC	RSLETTEPGY	LFDELNWCNG	SLTGNTKYGT		150
VCGCDYKSNV	VHAFWQSASA	EYARRASGNI	FVVLNGSVKA	PFENKTEGK		200
IELPLLKHPR	VOQLTVKLVH	SLEDVNNROT	CESWSLQELA	NKLSVHIPF		250
RCIDDPLEFR	HYQCIENPGK	QLCQFSASTR	SNVETLLILF	PLVICLTFYT		300
SMN						303

Figure 16 .

ATGATGAAYG	TNATHYTNTT	YYTNACNYTN	WSNAAYATHT	TYGTNTTYAA	50
YWSNGCNCAR	CAYCARATHA	AYYTNYTNWS	NGARATHGTN	CARWSNMGNT	100
GYACNCARTG	GAARGTNGAR	CAYGGNGCNA	CNAAYATHWS	NTGYWSNGAR	150
ATHTGGAAYW	SNTTYGARWS	NATHYTNYTN	WSNACNCAYA	CNAARWSNGC	200
NTGYGTNATG	AARWSNGGNY	TNTTYGAYGA	YTTYGTNTAY	CARYTNTTYG	250
ARYTNGARCA	RCARCARCAR	CARMGNCAYC	AYACNATHCA	RACNGARCAR	300
TAYTTYCAYW	SNCARGTNAT	GAAYATHATH	MGNGGNATGT	GYAARMGNYT	350
NGGNGTNTGY	MGNWSNYTNG	ARACNACNTT	YCCNGGNTAY	YTNTTYGAYG	400
ARYTNAAYTG	GTGYAAYGGN	WSNYTNACNG	GNAAYACNAA	RTAYGGNACN	450
GTNTGYGGNT	GYGAYTAYAA	RWSNAAYGTN	GTNCAYGCNT	TYTGGCARWS	500
NGCNWSNGCN	GARTAYGCNM	GNMGNGCNWS	NGGNAAYATH	TTYGTNGTNY	550
TNAAYGGNWS	NGTNAARGCN	CCNTTYAAYG	ARAAYAARAC	NTTYGGNAAR	600
ATHGARYTNC	CNYTNYTNAA	RCAYCCNMGN	GTNCARCARY	TNACNGTNAA	650
RYTNGTNCAY	WSNYTNGARG	AYGTNAAYAA	YMGNCARACN	TGYGARWSNT	700
GGWSNYTNCA	RGARYTNGCN	AAYAARYTNA	AYWSNGTNCA	YATHCCNTTY	750
MGNTGYATHG	AYGAYCCNYT	NGARTTYMGN	CAYTAYCART	GYATHGARAA	800
YCCNGGNAAR	CARYTNTGYC	ARTTYWSNGC	NWSNACNMGN	WSNAAYGTNG	850
ARACNYTNYT	NATHYTNTTY	CCNYTNGTNA	THTGYITNAC	NTTYTAYACN	900
WSNATGAAY					909

Figure 17